

Remarks

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I. Status

The present application was filed on October 24, 2001. Claims 1-62 have been subjected to a requirement for restriction. Specifically, the Examiner has concluded that these claims are directed to six separate and distinct inventions:

- I. Claims 1, 5-31,* drawn to a method for enhancing the dynamic range of an assay, classified in class 435, subclass 7.1;
- II. Claim 2, drawn to a method for enhancing the dynamic range of an assay, classified in class 436, subclass 63;
- III. Claims 3-4, drawn to a method for enhancing the dynamic range of an assay, classified in class 436, subclass 164;
- IV. Claims 32, 36-62,* drawn to an apparatus for enhancing the dynamic range of an assay, classified in class 422, subclass 82.07;
- V. Claim 33, drawn to an apparatus for enhancing the dynamic range of an assay, classified in class 422, subclass 104; and
- VI. Claims 34-35, drawn to an apparatus for enhancing the dynamic range of an assay, classified in class 435, subclass 808.

II. Response to Restriction Requirement

Applicants herewith elect to prosecute in this application the invention of Group I (claims 1, 5-31). Claims to the inventions of Groups IV – VI have therefore been cancelled.

* Applicants note that the Examiner's Action appears to have inadvertently failed to include claims 10-26 and 43-58 in *any* of the six cited Groups. Applicants submit that irrespective of whether these claims are generic or species claims, they must be categorized into one of the groups of claims in order to be examined in this application or in a divisional application. In light of the rationale advanced in the Examiner's Action, Applicants have considered the Examiner to have intended to place claims 10-26 in Group I and claims 43-58 in Group IV.

Applicants, however, respectfully request reconsideration of the Examiner's determination that the Inventions of Group I, II and III are separate and distinct from one another, and respectfully traverse this aspect of the Examiner's Action.

In this regard, Applicants respectfully submit that the claims of Groups I, II and III include related characteristics defining a single invention and should all be examined together. Specifically, the inventions of Groups I, II and III all concern a method for enhancing the dynamic range of an assay of the presence, absence, activity or concentration of two or more target analytes in one or more samples wherein the presence, absence, activity or concentration of said target analytes is assayed by the emission or quenching of a light signal. In all such claims, the method comprises causing a computer system to compare the generated data using data corresponding to the light signal generated by a known concentration of said target analyte in a known dynamic range of said assay and report the presence, absence, activity or concentration of said target analyte. The inventions of Groups II and III include all of the recitations of the invention of Group I, but provide additional definition as to how the recited CCD camera detector detects the light signal.

Applicants accordingly submit that Groups I, II and III do not define independent and distinct inventions. It is submitted that multiple searches would not be required should the Examiner combine Groups I, II and III for examination, and that no additional burden on the Examiner would result from examining the 3 additional claims of Groups II and III with those of Group I. Therefore, Applicants respectfully request that the Examiner amend the restriction requirement to combine the inventions of Groups I, II and III, and that claims 1-31 be examined in the present application.

III. Response to Requirement for Election of Species

The Examiner has stated that the claims are directed to patentably distinct species, and, with respect to elected claims 9-25, has required election of a single species for purposes of examination from the group:

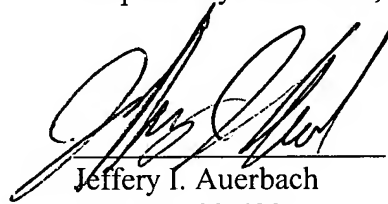
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|----|--------------------|----|----------------|
| A. | Enzyme | F. | A cytokine |
| B. | Drug or metabolite | G. | A blood factor |
| C. | A co-factor | H. | A virus |
| D. | A receptor | I. | An antigen |
| E. | A receptor ligand | J. | A steroid |
| F. | A hormone | K. | An antibody |

Applicants herewith respond to the requirement of r election of species by electing the species "cytokine" in claim 9. Interleukin-8 (IL-8) is a representative cytokine. Elected claims 9, and 16-17 read upon the elected species.

Having now fully responded to the Examiner's action, Applicants respectfully submit that the present application is in condition for Examination, and respectfully solicit early notice of favorable action. The Examiner is invited to contact the undersigned as to any matter arising in the prosecution of this application.

Respectfully Submitted,

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Appendix A: Nature of the Amendments

To facilitate the Examiner's review of the present Reply, the nature of the requested amendments is shown below.

Claims 1-31 Not Amended

32. **[Cancelled]** An apparatus for enhancing the dynamic range of an assay of the presence, absence, activity or concentration of two or more target analytes in one or more samples, wherein the presence, absence, activity or concentration of said target analytes is assayed by the emission or quenching of a light signal, said apparatus comprising:
- (A) one or more containers for receiving a portion of said one or more samples, said containers additionally containing assay reagents comprising a compound that, in response to the presence of a target analyte causes a detectable light signal; and
 - (B) a computer system comprising a CCD camera detector, said computer system being specially adapted to detect said light signal and generate data corresponding to said detected signal; said computer system additionally processing a capability for comparing said generated data with data corresponding to the light signal generated by a known concentration of said target analyte in a known dynamic range of said assay and report the presence, absence, activity or concentration of said target analyte; wherein said computer system causes said CCD camera detector to independently detect sufficient light signal for each of said target analytes to ensure that said reported presence, absence, activity or concentration of each target analyte is determined using data corresponding to a light signal that is within said known dynamic range of said assay for that target analyte.
33. **[Cancelled]** An apparatus for enhancing the dynamic range of an assay of the presence, absence, activity or concentration of two or more target analytes in one or more samples, wherein the presence, absence, activity or concentration of said target analytes is assayed by the emission or quenching of a light signal, said apparatus comprising:

- (A) one or more containers for receiving a portion of said one or more samples, said containers additionally containing assay reagents comprising a compound that, in response to the presence of a target analyte causes a detectable light signal; and
 - (B) a computer system comprising a CCD camera detector, said computer system being specially adapted to detect said light signal and generate data corresponding to said detected signal; said computer system additionally processing a capability for comparing said generated data with data corresponding to the light signal generated by a known concentration of said target analyte in a known dynamic range of said assay and report the presence, absence, activity or concentration of said target analyte; wherein said computer system causes said CCD camera detector to independently detect sufficient light signal for each of said target analytes to ensure that said reported presence, absence, activity or concentration of each target analyte is determined using data corresponding to a light signal that is within said known dynamic range of said assay for that target analyte; and wherein, for at least one of said target analytes, said computer system causes said CCD camera detector to detect light signal cumulatively until a total detected light signal is obtained that is within the known dynamic range of said assay for said target analyte; and wherein said total detected light signal is used to determine said presence, absence, activity or concentration of said target analyte.
34. **[Cancelled]** An apparatus for enhancing the dynamic range of an assay of the presence, absence, activity or concentration of two or more target analytes in one or more samples, wherein the presence, absence, activity or concentration of said target analytes is assayed by the emission or quenching of a light signal, said apparatus comprising:
- (A) one or more containers for receiving a portion of said one or more samples, said containers additionally containing assay reagents comprising a compound that, in response to the presence of a target analyte causes a detectable light signal; and
 - (B) a computer system comprising a CCD camera detector, said computer system being specially adapted to detect said light signal and generate data corresponding to said detected signal; said computer system additionally processing a capability

for comparing said generated data with data corresponding to the light signal generated by a known concentration of said target analyte in a known dynamic range of said assay and report the presence, absence, activity or concentration of said target analyte; wherein said computer system causes said CCD camera detector to independently detect sufficient light signal for each of said target analytes to ensure that said reported presence, absence, activity or concentration of each target analyte is determined using data corresponding to a light signal that is within said known dynamic range of said assay for that target analyte; and wherein, for at least one of said target analytes, said computer system causes said CCD camera detector to detect light signal discontinuously at more than one time interval so that a detected light signal is obtained that is within the known dynamic range of said assay for said target analyte; and wherein said detected light signal within the known dynamic range of said assay for said target analyte is used to determine said presence, absence, activity or concentration of said target analyte.

35. **[Cancelled]** The apparatus of claim 34, wherein said computer system stores the cumulative change in said light signal in two or more of said time intervals.
36. **[Cancelled]** The apparatus of claim 32, wherein said apparatus simultaneously assays the presence, absence, activity or concentration of said more than one target analyte in the same sample.
37. **[Cancelled]** The apparatus of claim 32, wherein said apparatus sequentially assays the presence, absence, activity or concentration of said more than one target analyte in the same sample.
38. **[Cancelled]** The method of claim 32, wherein said step (C) is performed simultaneously for each target analyte being assayed.
39. **[Cancelled]** The method of claim 32, wherein said step (C) is performed sequentially for each target analyte being assayed.

40. **[Cancelled]** The apparatus of claim 32, wherein said one or more containers is a multi-well microtiter plate.
41. **[Cancelled]** The apparatus of claim 32, wherein said target analyte has an activity and wherein said computer system additionally calculates the rate of a target analyte activity in said sample.
42. **[Cancelled]** The apparatus of claim 32, wherein said target analyte is selected from the group consisting of an enzyme, a drug or metabolite, a co-factor, a receptor, a receptor ligand, a hormone, a cytokine, a blood factor, a virus, an antigen, a steroid, and an antibody.
43. **[Cancelled]** The apparatus of claim 42, wherein said assay assays the presence, absence, activity or concentration of an enzyme.
44. **[Cancelled]** The apparatus of claim 43, wherein said enzyme is selected from the group consisting of bone specific alkaline phosphatase, aldose reductase, myoglobin, and troponin I.
45. **[Cancelled]** The apparatus of claim 42, wherein said assay assays the presence, absence, activity or concentration of a drug or metabolite.
46. **[Cancelled]** The apparatus of claim 45, wherein said drug or metabolite is selected from the group consisting of: an anti-cancer drug, chemotherapeutic drug, anti-viral drug, non-steroidal anti-inflammatory drug (NSAID), steroidal anti-inflammatory drug, anti-fungal drug, detoxifying drug, analgesic, bronchodilator, anti-bacterial drug, antibiotic drugs, diuretic, digoxin, anti-metabolite, calcium channel blocker, drug for treatment of psoriasis, and a substance of abuse.
47. **[Cancelled]** The apparatus of claim 42, wherein said assay assays the presence, absence, activity or concentration of a co-factor.
48. **[Cancelled]** The apparatus of claim 47, wherein said co-factor is a vitamin, T₃, or T₄.

49. **[Cancelled]** The apparatus of claim 42, wherein said assay assays the presence, absence, activity or concentration of a cytokine.
50. **[Cancelled]** The apparatus of claim 49, wherein said cytokine is IL-1 β , IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-12, IL-13, TNF α , VEGF, GMCSF, FGF β , INF γ , EGF, PDGF, MCSF, SCF, insulin, VEGF, Trk, Met, Ron, Axl, Eph, Fas, CD40, CD30, CD27, 4-1BB, LNGFR, OX40, TGF β R, or is a ligand of CCR1, CCR2 α , β , CCR3, CCR4, CCR5, CXCR1, CXCR2, CXCR3, CXCR4, BLR1, BLR2, or V28 receptor, or is a ligand of a receptor of IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-12, or IL-13.
51. **[Cancelled]** The apparatus of claim 42, wherein said assay assays the presence, absence, activity or concentration of a receptor or receptor ligand.
52. **[Cancelled]** The apparatus of claim 51, wherein said receptor or receptor ligand is 4-1BB, Axl, BLR1, BLR2, CCR1, CCR2 α , β , CCR3, CCR4, CCR5, CD27, CD30, CD4, CD40, CXCR1, CXCR2, CXCR3, CXCR4, EGFR, Eph, EPO receptor, Fas receptor, GCSFR, GHR, GMCSFR α , gp130, IFN γ R α , IFN γ R β , IFN α R1, insulin-R, IL-1 β , IL-2R β , IL-2R γ chains, IL-4R α , IL-3R α , IL-5R α , IL-6R α , IL-7R α , IL-9R α , IL-10R, IL-11R α , IL-12R β 1, IL-12R β 2, IL-13R α , GMCSFR α , IL-3/IL-5/GM-CSF receptor common β -chain, LIFR β , LNGFR, MCSFR, Met, OBR, OSMR β , OX40, PDGFR, PRL, Ron, SCFR, TPOR, TFR, TGF β R, TNFRI, TNFRII, TPOR, Trk, V28, VEGFR.
53. **[Cancelled]** The apparatus of claim 42, wherein said assay assays the presence, absence, activity or concentration of a hormone.
54. **[Cancelled]** The apparatus of claim 53, wherein said hormone is adrenaline, adrenocorticotrophic hormone, testosterone, angiotensinogen, antidiuretic hormone, atrial-natriuretic peptide, calcitonin, calcitriol, cholecystokinin, chorionic gonadotropin, cortisol, dopamine, erythropoietin, estradiol, follicle-stimulating hormone, gastrin, glucagon, gonadotropin-releasing hormone, corticotropin-releasing hormone, growth hormone, growth hormone-releasing hormone, insulin, insulin-like growth factor-1, leptin, luteinizing hormone, melatonin, aldosterone, neuropeptide Y, noradrenaline,

oxytocin, parathyroid hormone, progesterone, prolactin, renin, secretin, somatostatin, theophylline, triiodothyronine, thrombopoietin, thyroid-stimulating hormone, thyrotropin-releasing hormone, or thyroxine.

55. **[Cancelled]** The apparatus of claim 42, wherein said assay assays a binding activity of an antigen or an antibody.
56. **[Cancelled]** The apparatus of claim 55, wherein said assay assays a binding activity of an antigen characteristic of *Chlamydia*, *Streptococcus pyogenes* Group A bacteria, *H. pylori*, or *M. tuberculosis*, hepatitis virus, rubella, CMV, HIV, FIV, or prostate specific antigen, or an antibody elicited in response to any of such antigens.
57. **[Cancelled]** The apparatus of claim 42, wherein said assay assays a binding activity of an autoimmune immunoglobulin, thyroglobulin, anti-thyroglobulin, IgE, IgG, or IgM immunoglobulin.
58. **[Cancelled]** The apparatus of claim 42, wherein said assay assays a binding activity of a tumor marker.
59. **[Cancelled]** The apparatus of claim 32, wherein said light signal is an evolution or loss of a fluorescent light signal.
60. **[Cancelled]** The apparatus of claim 32, wherein said light signal is an evolution or loss of a chemiluminescent light signal.
61. **[Cancelled]** The apparatus of claim 32, wherein said light signal is an evolution or loss of an ultraviolet light signal.
62. **[Cancelled]** The apparatus of claim 32, wherein said light signal is an evolution or loss of a visible wavelength light signal.

Appendix B: The Pending Claims

To facilitate the Examiner's review of the present Reply, the pending claims are shown below.

1. A method for enhancing the dynamic range of an assay of the presence, absence, activity or concentration of two or more target analytes in one or more samples wherein the presence, absence, activity or concentration of said target analytes is assayed by the emission or quenching of a light signal, wherein said method comprises the steps:
 - (A) conducting an assay for the presence, absence, activity or concentration of each of said target analytes in said one or more samples wherein said assays each cause light signals to be emitted or quenched;
 - (B) employing a computer system comprising a CCD camera detector to detect said light signals, and to generate data corresponding to said detected signals; and
 - (C) causing said computer system to compare said generated data using data corresponding to the light signal generated by a known concentration of said target analyte in a known dynamic range of said assay and report the presence, absence, activity or concentration of said target analyte; wherein said computer system causes said CCD camera detector to independently detect sufficient light signal for each of said target analytes to ensure that said reported presence, absence, activity or concentration of each target analyte is determined using data corresponding to a light signal that is within said known dynamic range of said assay for that target analyte.
2. A method for enhancing the dynamic range of an assay of the presence, absence, activity or concentration of two or more target analytes in one or more samples wherein the presence, absence, activity or concentration of said target analytes is assayed by the emission or quenching of a light signal, wherein said method comprises the steps:

- (A) conducting an assay for the presence, absence, activity or concentration of each of said target analytes in said one or more samples wherein said assays each cause light signals to be emitted or quenched;
 - (B) employing a computer system comprising a CCD camera detector to detect said light signals, and to generate data corresponding to said detected signals; and
 - (C) causing said computer system to compare said generated data using data corresponding to the light signal generated by a known concentration of said target analyte in a known dynamic range of said assay and report the presence, absence, activity or concentration of said target analyte; wherein said computer system causes said CCD camera detector to independently detect sufficient light signal for each of said target analytes to ensure that said reported presence, absence, activity or concentration of each target analyte is determined using data corresponding to a light signal that is within said known dynamic range of said assay for that target analyte; and wherein, for at least one of said target analytes, said computer system causes said CCD camera detector to detect light signal cumulatively until a total detected light signal is obtained that is within the known dynamic range of said assay for said target analyte; and wherein said total detected light signal is used to determine said presence, absence, activity or concentration of said target analyte.
3. A method for enhancing the dynamic range of an assay of the presence, absence, activity or concentration of two or more target analytes in one or more samples wherein the presence, absence, activity or concentration of said target analytes is assayed by the emission or quenching of a light signal, wherein said method comprises the steps:
- (A) conducting an assay for the presence, absence, activity or concentration of each of said target analytes in said one or more samples wherein said assays each cause light signals to be emitted or quenched;
 - (B) employing a computer system comprising a CCD camera detector to detect said light signals, and to generate data corresponding to said detected signals; and

- (C) causing said computer system to compare said generated data using data corresponding to the light signal generated by a known concentration of said target analyte in a known dynamic range of said assay and report the presence, absence, activity or concentration of said target analyte; wherein said computer system causes said CCD camera detector to independently detect sufficient light signal for each of said target analytes to ensure that said reported presence, absence, activity or concentration of each target analyte is determined using data corresponding to a light signal that is within said known dynamic range of said assay for that target analyte; and wherein, for at least one of said target analytes, said computer system causes said CCD camera detector to detect light signal discontinuously at more than one time interval so that a detected light signal is obtained that is within the known dynamic range of said assay for said target analyte; and wherein said detected light signal within the known dynamic range of said assay for said target analyte is used to determine said presence, absence, activity or concentration of said target analyte.
4. The method of claim 3, wherein said computer system stores the cumulative change in said light signal in two or more of said time intervals.
 5. The method of claim 1, wherein said method simultaneously assays the presence, absence, activity or concentration of two or more of said target analytes in said sample.
 6. The method of claim 1, wherein said method sequentially assays the presence, absence, activity or concentration of two or more of said target analytes in said sample.
 7. The method of claim 1, wherein said step (C) is performed simultaneously for each target analyte being assayed.
 8. The method of claim 1, wherein said step (C) is performed sequentially for each target analyte being assayed.

9. The method of claim 1, wherein at least one of said target analyte is selected from the group consisting of an enzyme, a drug or metabolite, a co-factor, a receptor, a receptor ligand, a hormone, a cytokine, a blood factor, a virus, an antigen, a steroid, and an antibody.
10. The method of claim 9, wherein said assay assays the presence, absence, activity or concentration of an enzyme.
11. The method of claim 10, wherein said enzyme is selected from the group consisting of bone specific alkaline phosphatase, aldose reductase, myoglobin, and troponin I.
12. The method of claim 9, wherein said assay assays the presence, absence, activity or concentration of a drug or metabolite.
13. The method of claim 12, wherein said drug or metabolite is selected from the group consisting of: an anti-cancer drug, chemotherapeutic drug, anti-viral drug, non-steroidal anti-inflammatory drug (NSAID), steroidal anti-inflammatory drug, anti-fungal drug, detoxifying drug, analgesic, bronchodilator, anti-bacterial drug, antibiotic drugs, diuretic, digoxin, anti-metabolite, calcium channel blocker, drug for treatment of psoriasis, and a substance of abuse.
14. The method of claim 9, wherein said assay assays the presence, absence, activity or concentration of a co-factor.
15. The method of claim 14, wherein said co-factor is a vitamin, T₃, or T₄.
16. The method of claim 9, wherein said assay assays the presence, absence, activity or concentration of a cytokine.
17. The method of claim 16, wherein said cytokine is IL-1 β , IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-12, IL-13, TNF α , VEGF, GMCSF, FGF β , INF γ , EGF, PDGF, MCSF, SCF, insulin, VEGF, Trk, Met, Ron, Axl, Eph, Fas, CD40, CD30, CD27, 4-1BB, LNGFR, OX40, TGF β R, or is a ligand of CCR1, CCR2 α , β , CCR3, CCR4, CCR5,

CXCR1, CXCR2, CXCR3, CXCR4, BLR1, BLR2, or V28 receptor, or is a ligand of a receptor of IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-12, or IL-13.

18. The method of claim 9, wherein said assay assays the presence, absence, activity or concentration of a receptor or receptor ligand.
19. The method of claim 18, wherein said receptor or receptor ligand is 4-1BB, Axl, BLR1, BLR2, CCR1, CCR2 α , β , CCR3, CCR4, CCR5, CD27, CD30, CD4, CD4, CD40, CXCR1, CXCR2, CXCR3, CXCR4, EGFR, Eph, EPO receptor, Fas receptor, GCSFR, GHR, GMCSFR α , gp130, IFN γ R α , IFN γ R β , IFN α R1, insulin-R, IL-1 β , IL-2R β , IL-2R γ chains, IL-4R α , IL-3R α , IL-5R α , IL-6R α , IL-7R α , IL-9R α , IL-10R, IL-11R α , IL-12R β 1, IL-12R β 2, IL-13R α , GMCSFR α , IL-3/IL-5/GM-CSF receptor common β -chain, LIFR β , LNGFR, MCSFR, Met, OBR, OSMR β , OX40, PDGFR, PRL, Ron, SCFR, TPOR, TFR, TGF β R, TNFR1, TNFR2, TPOR, Trk, V28, VEGFR
20. The method of claim 9, wherein said assay assays the presence, absence, activity or concentration of a hormone.
21. The method of claim 20, wherein said hormone is adrenaline, adrenocorticotrophic hormone, testosterone, angiotensinogen, antidiuretic hormone, atrial-natriuretic peptide, calcitonin, calcitriol, cholecystokinin, chorionic gonadotropin, cortisol, dopamine, erythropoietin, estradiol, follicle-stimulating hormone, gastrin, glucagon, gonadotropin-releasing hormone, growth hormone-releasing hormone, growth hormone, growth hormone-releasing hormone, insulin, insulin-like growth factor-1, leptin, luteinizing hormone, melatonin, aldosterone, neuropeptide Y, noradrenaline, oxytocin, parathyroid hormone, progesterone, prolactin, renin, secretin, somatostatin, theophylline, triiodothyronine, thrombopoietin, thyroid-stimulating hormone, thyrotropin-releasing hormone, or thyroxine.
22. The method of claim 9, wherein said assay assays a binding activity of an antigen or an antibody.

23. The method of claim 22, wherein said assay assays a binding activity of an antigen characteristic of *Chlamydia*, *Streptococcus pyogenes* Group A bacteria, *H. pylori*, or *M. tuberculosis*, hepatitis virus, rubella, CMV, HIV, FIV, or prostate specific antigen, or an antibody elicited in response to any of such antigens.
24. The method of claim 9, wherein said assay assays a binding activity of an autoimmune immunoglobulin, thyroglobulin, anti-thyroglobulin, IgE, IgG, or IgM immunoglobulin.
25. The method of claim 9, wherein said assay assays a binding activity of a tumor marker.
26. The method of claim 1, wherein said light signal is an evolution or loss of a fluorescent light signal.
27. The method of claim 1, wherein said light signal is an evolution or loss of a chemiluminescent light signal.
28. The method of claim 1, wherein said light signal is an evolution or loss of an ultraviolet light signal.
29. The method of claim 1, wherein said light signal is an evolution or loss of a visible wavelength light signal.
30. The method of claim 1, wherein said assays are conducted in a multi-well microtiter plate.
31. The method of claim 1, wherein a target analyte has an activity and wherein said computer system additionally calculates the rate of activity of said target analyte in said sample.